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EXAMINER

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ART UNIT	PAPER NUMBER
1642	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/462,625	GEORGIEV ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 03 December 2001.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-52 is/are pending in the application.

4a) Of the above claim(s) 24-52 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-23 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) 1-52 are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. _____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3,11 . 6) Other: *Notice to Comply* .

DETAILED ACTION

1. The election with traverse filed December 3, 2001 in Paper No. 12 is acknowledged and has been entered.
2. Claims 1-52 are pending in the application. Claims 24-52 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 12.
3. Claims 1-23 are currently under prosecution.

Priority

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Election/Restrictions

5. Applicant's election with traverse of Group I, claims 1-23 in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the invention of Groups I-V are closely related and therefore no serious burden would be imposed upon the Examiner if the restriction were not made. This is not found persuasive because as stated in the Office Action mailed October 2, 2001 (Paper No. 9), Groups I-V do not share the same or corresponding special technical feature and are not so linked as to form a single general inventive concept. Furthermore, as this application is filed under 35 USC § 371, PCT Rules 13.1 and 13.2 do not provide for a single inventive concept comprising more than the first claimed product, the first claimed method for making the product, and the first claimed method for using the product. Nonetheless, contrary to Applicants'

assertion, the search required for each different group is not co-extensive with the search required for any other group; therefore, different searches are required for each group and to examine more than one group would constitute a serious burden.

The requirement is still deemed proper and is therefore made FINAL.

Objections for Lack of Compliance with the Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

In particular, it is noted that on page 81, line 17, the specification identifies a sequence as SEQ ID NO: 4, which is not identical to the sequence of SEQ ID NO: 4 in the Sequence Listing. On page 49, line 17, again, the specification identifies a sequence as SEQ ID NO: 4, which is not identical to the sequence of SEQ ID NO: 4 in the Sequence Listing. Similarly, on page 56, line 27, the specification identifies a sequence as SEQ ID NO: 3, which is not identical to the sequence of SEQ ID NO: 3 in the Sequence Listing. As this is probably not an exhaustive or complete list of the errors, Applicants are advised to confirm that the specification and the Sequence Listing are fully correspondent.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be further examined under 35 U.S.C. §§ 131 and 132.

Applicant is given the same period time with which to reply to this Office Action to place the application in compliance with 37 CFR §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Applicants are requested to return a copy of the attached Notice to Comply with the response.

Claim Objections

7. Claims 1 and 22 are objected to because of the following informalities:
 - (a) Claim 1 is objected to because claim 1 is not punctuated with a period at the end of the sentence. Appropriate correction is required.
 - (b) Claim 22 is objected to because there is no space between "claims" and "18" in line 1 of the claim. Appropriate correction is required.
8. Claims 14, 16, 21, and 22 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 101

9. Claim 16 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 16 is drawn to a host cell comprising the nucleic acid molecule of claim 1, claim 8, or claim 11.

Claim 16 encompasses a naturally occurring product, since the definition of a host cell is not limiting and because claims 1 and 8 encompass isolated naturally occurring genomic DNA molecules and isolated naturally occurring messenger RNA (mRNA) molecules. For example, a mouse cell comprises a nucleic acid of claim 1 or claim 8. As claim 16 is written, the subject matter of the claim is not distinguished from such a naturally occurring product.

Amending claim 16 to recite, for example, the term "transfected" or "transformed" before "host cell" can obviate this rejection, but Applicants are cautioned against the introduction of new matter.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1, 2, 6, 7, 9, 10, and 12-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising SEQ ID NO: 1, the complement or a fragment of said nucleic acid molecule, an isolated nucleic acid molecule encoding the polypeptide of SEQ ID NO: 2, a vector comprising a nucleic acid molecule comprising SEQ ID NO: 1, a host cell comprising said vector, a method for producing a polypeptide comprising culturing said host cell, an isolated polypeptide comprising SEQ ID NO: 2, and an antigenic fragment of said polypeptide does not reasonably provide enablement for an isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence that is at least 65% but less than 100% identical to SEQ ID NO: 1, the complement or a fragment of said nucleic acid molecule, an isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence that is at least 65% but less than 100% identical to a nucleotide sequence encoding the polypeptide of SEQ ID NO: 2, a vector comprising a nucleic acid molecule comprising a polynucleotide having a nucleotide sequence that is at least 65% but less than 100% identical to SEQ ID NO: 1, a host cell comprising said vector, a method for producing a polypeptide comprising culturing said host cell, an isolated polypeptide comprising an amino acid sequence at least 65% identical but less than 100% identical to SEQ ID NO: 2, and an antigenic fragment of said polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because one skilled in the art could not make or use the claimed invention with a reasonable expectation of success without having to perform undue experimentation. Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI

1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification provides sufficient guidance and direction, together with working exemplification, to enable the skilled artisan to make and use the isolated nucleic acid molecule comprising SEQ ID NO: 1, which the specification teaches encodes the polypeptide of SEQ ID NO: 2; however, the claimed invention encompasses a much broader genus of isolated nucleic acids having undisclosed polynucleotide sequences, which according to the claims are only required to share at least 65% of the nucleotide residues with SEQ ID NO: 1, presumably after an optimal alignment of the two sequences for comparison using an appropriate computer algorithm. Therefore, the claims encompass any and all isolated nucleic acid molecules that differ in polynucleotide sequence from SEQ ID NO: 1 at no greater than 65 nucleotide positions out of every 100, or in other words, as many as 35 residues out every 100 can be different from SEQ ID NO: 1, but still the nucleic acid molecule falls within the scope of the claims. With each and every discrepant nucleotide residue, the predictability that the claimed nucleic acid molecule will function similarly enough to the isolated nucleic acid comprising SEQ ID NO: 1 for this instant disclosure to be considered enabling declines significantly. In fact, even a single nucleotide alteration in a polynucleotide sequence can result in the alteration of the amino acid sequence of a protein, and even a single alteration in the amino acid sequence of a protein can drastically alter the function of the protein. Bowie, et al (*Science* **257**: 1306-1310, 1990) teach that an amino acid sequence encodes a message that determines the shape and function of a protein; and, that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome. Even if the skilled artisan were able to submit a complete list of the possible nucleic acids and the proteins encoded thereby, which fall within the scope of the claims, the skilled artisan could not predict which of these would function similarly to the

nucleic acid comprising SEQ ID NO: 1 and the protein encoded thereby comprising SEQ ID NO: 2, and which would not, because Bowie, et al teach that the prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (page 1306, column 1). Bowie, et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship and these regions can tolerate only conservative substitutions or none at all (page 1306, column 2). In this regard, it is noted that the specification does not teach which amino acid residues are critical to the function of the protein comprising SEQ ID NO: 2, and moreover, does not teach which amino acids can be used to replace critical residues in the protein so that the resultant protein retains the function of the protein comprising SEQ ID NO: 2. Because the specification fails to provide essential guidance and direction and because the art is so highly unpredictable, the skilled artisan would only be able to empirically determine whether members of the claimed genus of nucleic acid molecules encode proteins that have similar or identical function to the protein encoded by SEQ ID NO: 1, and therefore, the skilled artisan could not make or use the invention with a reasonable expectation of success without first having to perform undue experimentation.

In further support of the high degree of unpredictability and the consequent need to perform undue experimentation to make and use the claimed invention with a reasonable expectation of success in the absence of a sufficient disclosure, which includes working exemplification, guidance, and direction that is reasonably commensurate in scope with the claims, Burgess, et al (*Journal of Cell Biology* 111: 2129-2138, 1990) exemplifies the sensitivity of proteins to alterations of even a single amino acid in a sequence. Burgess, et al teach that replacement of a single lysine reside at position 118 of acidic fibroblast growth factor by glutamic acid led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. As another example, Lazar et al (*Molecular and Cellular Biology*, 1988, 8: 1247-1252)

teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect but that a replacement with serine or glutamic acid sharply reduced its biological activity. Thus, as evident from the teaching of Lazar, et al, even a single conservative type amino acid substitution may adversely affect the function of a protein, and yet, in a protein the size of tag7, which is encoded by SEQ ID NO: 1, about 64 amino acids could be replaced in the amino acid sequence of SEQ ID NO: 2 and still the protein would fall within the scope of the claims.

Considering the teachings of the references cited above, it is apparent that even a single amino acid substitution can dramatically affect the biological activity and the structure-function characteristics of a protein. Therefore, the skilled artisan would not immediately conclude that any of the claimed proteins, except that comprising the amino acid sequence set forth in SEQ ID NO: 2, encoded by one of the many nucleic acid molecules encompassed by the claims will have a biological activity that is identical or even similar to the protein comprising SEQ ID NO: 2, simply because the claims require the polynucleotide sequences encoding the claimed proteins to be at least 65% identical to the nucleotide sequence set forth in SEQ ID NO: 1, or because the claims require the amino acid sequence of the claimed proteins to be at least 65% identical to the polypeptide sequence set forth in SEQ ID NO: 2. Based upon the teachings of Bowie, et al, Burgess, et al, and Lazar, et al, it is especially evident that one skilled in the art cannot predict whether the broadly claimed nucleic acid molecules encoding proteins that have an amino acid sequence that is less than 100% identical to SEQ ID NO: 2 will function the same as the protein comprising SEQ ID NO: 2, but if the claimed proteins do not function identically or at least highly similarly to the protein comprising SEQ ID NO: 2, it is apparent that the specification does not teach how such proteins can be made or used and therefore the specification is not reasonably enabling of the claimed invention.

With regard to the claimed nucleic acid molecule comprising SEQ ID NO: 3, which encodes a protein comprising the amino acid sequence set forth in SEQ ID NO: 4, although clearly the claimed nucleic acid molecule and claimed protein can be made in view of the disclosure, it is noted that the specification does not teach or exemplify

their use, and more particularly, fails to demonstrate that the protein comprising SEQ ID NO: 4 has the same or similar biological activity as the protein comprising SEQ ID NO: 2. Since the protein is only 66.1% similar to the protein comprising SEQ ID NO: 2 (page 74, lines 3-6), based upon the state of the art as evidenced by the teachings of Bowie, Burgess, et al, and Lazar, et al, is evident that in the absence of working exemplification and/or specific teachings, that the skilled artisan cannot predict whether the protein comprising SEQ ID NO: 4 will have the same or similar biological activity as the protein comprising SEQ ID NO: 2. Therefore, again, the teaching and exemplification in the specification is not reasonably commensurate in scope with the claims, especially those claims limited to the isolated nucleic acid comprising SEQ ID NO: 3 or the isolated protein comprising SEQ ID NO: 4.

In summary, the specification fails to meet the enablement requirement of 35 USC § 112, first paragraph because the disclosed teachings, guidance, direction, and exemplification is not reasonably commensurate in scope with the claims and therefore one skilled in the art could not make and/or use the claimed invention with a reasonable expectation of success without having to first perform undue experimentation.

12. Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The teachings of the specification cannot be extrapolated to the enablement of the claimed invention because there are a number of discrepancies between the polynucleotide sequences disclosed in the specification and the corresponding polynucleotide sequences reported in the literature or submitted to publicly accessible databases.

In particular, according to Kiselev, et al (*Journal of Biological Chemistry* 273: 18633-18639, 1998; Form PTO-1449, citation no. 10-AS), the polynucleotide sequence encoding mouse tag7 protein (GenBank Accession No. X86374; Form PTO-1449, citation no. 11-AT) differs from the polynucleotide sequence, i.e., SEQ ID NO: 1, which

the specification teaches encodes mouse tag7 protein. A comparison of the two polynucleotide sequences, which supposedly encode the same protein, reveals differences, including one mismatched residue and an insertion of two additional residues in SEQ ID NO: 1, which are absent in the GenBank sequence. Because of these differences, the polynucleotide sequence set forth as GenBank Accession No. X86374 does not encode a protein comprising the amino acid sequence set forth in SEQ ID NO: 2. Furthermore, according to Kiselev, et al, the polynucleotide sequence within the coding sequence of the first intron of the gene encoding mouse tag7 (GenBank Accession No. Y12088) also differs from the polynucleotide sequence set forth in SEQ ID NO: 1, although this discrepancy might be more readily explained since the sequence differences occur at or near the probable splice junction.

In light of these discrepancies and/or errors, there is a reasonable doubt that the disclosure of the invention meets the enablement requirement of 35 USC § 112, first paragraph. Any inaccuracies in the polynucleotide or polypeptide sequences disclosed in the specification would preclude the successful practice (i.e., production and/or use) of the invention. The specification apparently offers no disclosure that might explain these discrepancies or serve to instruct the practitioner that the polynucleotide sequences reported elsewhere are considered to be inaccurate. The disclosure, therefore, would not enable the skilled artisan to make and use the claimed invention with a reasonable expectation of success without having to first perform undue experimentation.

Furthermore, with particular regard to claims 1, 5, and 19, while claims 1 and 19 define "the mature tag7 polypeptide" as having the amino acid sequence set forth at positions 20 to 182 in SEQ ID NO: 2, claim 5 inconsistently defines the mature tag7 polypeptide as having the amino acid sequence at positions 13 to 182 in SEQ ID NO: 2. The specification fails to clarify the inconsistency, vaguely teaching "the mature tag7 polypeptide may or may not differ from the 'mature' tag7 polypeptide shown in Figure 1 (SEQ ID NO:2 ; amino acids from about 20 to about 182) depending upon the accuracy of the predicted cleavage site based on computer analysis (page 16, lines 19-22) and "depending upon the accuracy of this analysis the cleavage site may be expected to be

anywhere from about amino acid 10 to about amino acid 30" (page 16, lines 28 and 29). Nonetheless, the mature protein will consist of a particular subsequence of SEQ ID NO: 2, but cannot have the amino acid sequence of SEQ ID NO: 2 from 13 to 182, if the mature protein actually consists of amino acids 20 to 182 of SEQ ID NO: 2. Therefore, in view of the ambiguity of the claims and the disclosure, one skilled in the art would not be able to make and/or use the claimed invention with a reasonable expectation of success without first having to perform undue experimentation.

Amendment of the claims and specification to resolve the discrepancies may be required; however, Applicant is cautioned against the introduction of new matter if amendments and/or corrections are made to the specification, including the claims, the figures, and the Sequence Listing.

13. Claims 1, 2, 4-10, and 12-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description sets forth SEQ ID NO: 1 and SEQ ID NO: 3, which are the open reading frame (ORF) of or the polynucleotide sequence of cDNA molecules isolated from mouse and human, respectively, and are purported to encode polypeptides having the amino acid sequences set forth in SEQ ID NO: 2 and SEQ ID NO: 4, respectively. The claims, however, encompass a broad genus of isolated nucleic acid molecules having at least 65% identity to the polynucleotide sequence set forth in SEQ ID NO: 1. Therefore, the claims encompass naturally occurring genomic DNA, including allelic variants, messenger RNA (mRNA), including differentially spliced mRNA, and other cDNA molecules derived from the variously spliced mRNA molecules encoded by allelic variants, homologs, paralogs, or orthologs of the gene encoding mouse tag7 protein comprising the amino acid sequence set forth in SEQ ID NO: 2. The structures and polynucleotide sequences of the vast majority of these congeneric species of nucleic acid molecules are not disclosed in the specification and the disclosure of two isolated species of the claimed genus of nucleic acid molecules,

namely SEQ ID NO: 1 and SEQ ID NO: 3, is considered insufficient to meet the written description requirement of 35 USC § 112, first paragraph. Moreover, the claims encompass a broad genus of isolated polypeptides having an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2, but apart from SEQ ID NO: 2, the specification only discloses the amino acid sequence of SEQ ID NO: 4 and consequently the written description is not reasonably commensurate with the claims and would not therefore reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the *invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*” (page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (page 115).

Furthermore, in *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement that defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “[a]n adequate written description of a DNA [molecule] ‘requires a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”.

Accordingly, the description of two species of the claimed genus, which are the polynucleotide sequences of cDNA molecules isolated from mouse and human, is not sufficient to enable one skilled in the art to recognize the other members of the claimed genus and to distinguish those members from the nucleic acid molecules that are not

claimed. Although the claims recite the requirement that the members of the claimed genus share at least 65% identity and hybridize to the a polynucleotide having the sequence set forth in SEQ ID NO: 1 under stringent or other defined hybridization conditions, this recitation merely states what the claimed species of the genus must do, rather than describing what they are. Otherwise, however, the specification fails to describe any other feature shared by each and every member of the claimed genus that might serve to enable one skilled in the art to recognize that, which is claimed, from that, which is not. While it is not necessary to describe each and every member of a claimed genus, it is necessary to describe a representative number of the members of the claimed genus, particularly if the specification fails to disclose a defining characteristic that distinguishes the members of the genus from others. Again the claims encompass naturally occurring genomic DNA, including allelic variants, messenger RNA (mRNA), including differentially spliced mRNA, and other cDNA molecules derived from the variously spliced mRNA molecules encoded by allelic variants, homologs, paralogs, or orthologs, which might be isolated from any other animal, provided that the nucleic acid molecule comprises a polynucleotide sequence that is at least 65% identical to the polynucleotide sequence set forth in SEQ ID NO: 1 or else encodes a protein having an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2; but representative numbers of these members of the claimed genus have not been described in the specification and in the absence of adequate description, one skilled in the art cannot immediately envision the structures or features of each.

Furthermore, the isolated naturally occurring genomic DNA molecules (i.e., the gene and its allelic variants), which encode the polypeptide having the amino acid sequence set forth in SEQ ID NO: 2, would be expected to have introns and exons as well as regulatory elements. The structures of these genomic DNA molecules encoding the polypeptide having the amino acid sequence that is at least 65% identical to the amino acid set forth in SEQ ID NO: 2 are not conventionally known in the art. Moreover, the specification fails to identify and describe the structures of the 5'- and 3'-regulatory regions contained within the untranslated regions, the polynucleotide

sequences of the introns, and the boundaries of the intron and exons that are essential to the function of the invention. In fact, the structures of naturally occurring genes with regulatory elements, untranslated regions, and introns and exons can only be determined empirically. Clearly, it is not possible to work backward from the known structure of a cDNA molecule to derive the unknown structure of the corresponding gene, which encodes the same polypeptide as the cDNA. See, for example, Harris et al, *Journal of the American Society of Nephrology*, 6: 1125-1133, 1995; Ahn et al, *Nature Genetics*, 3: 283-291, 1993; and Cawthon et al, *Genomics* 9: 446-460, 1991. Accordingly, in the absence of an adequate written description of a representative number of the species from within the claimed genus, the skilled artisan would not recognize from the disclosure that Applicant was in possession of the claimed genus of nucleic acids.

Furthermore, Applicant is reminded that conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

With regard to the claimed genus of polypeptides, although the claims are drawn to isolated naturally occurring amino acid sequence variants of the protein comprising SEQ ID NO: 2, which share at least 65% identity with SEQ ID NO: 2, and which are encoded by any of the many different species of nucleic acid molecules also claimed in this application, including allelic variants of the mouse and human genes encoding SEQ ID NO: 2 and the homologous genes and allelic variants of other species of animals, the specification only discloses the amino acid sequence of two species, namely SEQ ID NO: 2 and SEQ ID NO: 4. Again, the specification fails to describe any structural or functional characteristic or essential common feature of the members of claimed genus of proteins, which would serve to distinguish these two proteins and the other members of the claimed genus from proteins that are not claimed. The skilled artisan cannot envision the structures of the members of the claimed genus that have not been described in the specification and the number of members that have been described is not considered a representative number. Additionally, the specification actually only teaches that SEQ ID NO: 2 and SEQ ID NO: 4 are similar, but similarity is not defined in

the specification; and so, it is not clear whether SEQ ID NO: 4 is descriptive of the claimed genus, since it cannot be determined from the disclosure whether SEQ ID NO: 4 is at least 65% identical to SEQ ID NO: 2. The “similarity” of two optimally aligned amino acid sequences is not often synonymous with the “identity” of those sequences, because “similarity” permits the sequences to differ provided that the amino acid variation is conservative in nature. Therefore, the specification may have only described a single species of the claimed genus of polypeptides, rather than two.

In summary, adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required; and by analogy, if the structure of the nucleic acid encoding a polypeptide is unknown, the structure of the claimed polypeptide itself must have been described to reasonably convey to the skilled artisan that Applicants had possession of the claimed invention at the time the application was filed. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. With the exception of SEQ ID NO: 1 and SEQ ID NO: 3, the skilled artisan cannot immediately envision the detailed structure of the encompassed polynucleotides. With the exception of SEQ ID NO: 2 and SEQ ID NO: 4, the skilled artisan cannot immediately envision the detailed structure of the encompassed polypeptides. Consequently, the disclosure is insufficient to meet the written description requirement of 35 USC 112, first paragraph and to support the generic claims in accordance with *The Guidelines for Examination of Patent Applications* (66 FR 1099-1111, 5 January 2001).

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7 and 9-18 are indefinite because claim 1 recites the phrase "a fragment thereof" in line 17. Recitation of the phrase renders the claim indefinite because it is unclear whether the phrase refers to a fragment of the nucleotide sequence complementary to any one of the nucleotide sequences of (a), (b), (c), (d), or (e), or alternatively to a fragment of one of the nucleotide sequences of (a), (b), (c), (d), or (e). Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claims 1-7 and 9-18 are indefinite because claims 1 recites the phrase "the mature tag7 polypeptide having the amino acid sequence at positions 20 to 182 of SEQ ID NO: 2" while claim 5 recites, "the mature tag7 polypeptide having the amino acid sequence at positions 13 to 182 in SEQ ID NO: 2". While a mature tag7 polypeptide can have the amino acid sequence at positions 13 to 182 and also have the amino acid sequence at position 20 to 182 of SEQ ID NO: 2, a mature tag7 polypeptide cannot have the amino acid sequence at position 20 to 182 of SEQ ID NO: 2 and also have the amino acid sequence at positions 13 to 182 of SEQ ID NO: 2. The claims are therefore incongruous and accordingly one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claims 1-7 and 9-18 are indefinite because claim 1 recites the term "a tag7-encoding polypeptide" in lines 9 and 12. Recitation of the term renders the claim indefinite because the term is not defined in the claim or in the specification and therefore it cannot be ascertained to what subject matter the term in the claim refers. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claims 6 and 7 are indefinite for the same reason. Amending claims 1, 6, and 7 to delete the phrase "of a tag7-encoding polypeptide" can obviate this rejection.

Claims 8-18 and 20-23 are indefinite because claim 18 recites the phrases "consisting essentially of amino acids residues from about 20 to about 40", "consisting essentially of amino acids residues from about 55 to about 75", "consisting essentially of amino acids residues from about 90 to about 110", and "consisting essentially of amino acids residues from about 145 to about 160". Recitation of the phrase renders the claim

indefinite because it is inconsistent to state, for example, that the amino acid sequence of a polypeptide consists *essentially* of a fragment consisting of **about** residue 55 to **about** residue 75 of SEQ ID NO: 2, because the claim fails to distinctly set forth the *essential* sequence. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claims 10, 11, 14-18, and 20-23 are indefinite because claim 10 recites the limitation "wherein said nucleic acid molecule is isolated from a human". Recitation of the limitation renders the claim indefinite because the nucleic acid to which claim 8 refers, i.e., the nucleic acid molecule encoding an epitope bearing portion of SEQ ID NO: 2, is derived from the sequence of a nucleic acid molecule isolated from a mouse. The nucleic acid isolated from human, i.e., the nucleic acid encoding SEQ ID NO: 4, does not encode a polypeptide consisting essentially of amino acid residues from about 20 to about 40, from about 55 to about 75, from about 90 to about 110, or from about 145 to about 160; therefore, it appears that the isolated nucleic acid to which claim 10 refers cannot be isolated from a human.

Claims 19-23 are indefinite because claim 19 recites the phrase "a fragment thereof" in line 15. Recitation of the phrase renders the claim indefinite because it is unclear whether the phrase refers to a fragment of the amino acid sequence encoded by a polynucleotide that hybridizes under defined conditions to a polynucleotide having a nucleotide sequence set forth in SEQ ID NO: 1, or alternatively to a fragment of a polynucleotide having a nucleotide sequence set forth in SEQ ID NO: 1. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claims 19-23 are indefinite because claims 19 recites the phrase "the mature tag7 polypeptide having the amino acid sequence as set forth at positions 20 to 182 of SEQ ID NO: 2" while claim 5 recites, "the mature tag7 polypeptide having the amino acid sequence at positions 13 to 182 in SEQ ID NO: 2". While a mature tag7 polypeptide can have the amino acid sequence at positions 13 to 182 and also have the amino acid sequence at position 20 to 182 of SEQ ID NO: 2, a mature tag7 polypeptide cannot have the amino acid sequence at position 20 to 182 of SEQ ID NO: 2 and also

have the amino acid sequence at positions 13 to 182 of SEQ ID NO: 2. The claims are therefore incongruous and accordingly one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

17. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. Claims 3 and 4 are given benefit of the filing date of the earliest filed application to which this application claims benefit, i.e., US Application No. 08/893,764, (now US Patent No. 6,172,211-B1), which was filed July 11, 1997. However, claims 1, 2, and 5-23 are given only the benefit of the filing date of PCT/EP98/04287, which was filed July 10, 1998, because the present claims encompass subject matter that was not sufficiently supported by the disclosure of US Application No. 08/893,764 to meet the requirements of 35 USC § 112, first paragraph.

19. Claims 1, 2, 6-9, and 12-21 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over WO 97/29765-A1.

WO 97/29765-A1 teaches the polynucleotide sequence of a nucleic acid molecule isolated from mouse that encodes a polypeptide comprising an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2, which is designated murine granulocyte peptide A (MGP-A). Also, the nucleic acid molecule of WO 97/29765-A1 encodes an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 20 to about 40 of SEQ ID NO: 2, an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 55 to about 75 of SEQ ID NO: 2, an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 90 to about 110 of SEQ ID NO: 2, and an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 145 to about 160 of SEQ ID NO: 2. Additionally, the nucleic acid molecule of WO 97/29765-A1 is at least 65% identical to the polynucleotide sequence of SEQ ID NO: 1. Finally, WO 97/29765-A1 teaches vectors, including expression vectors, host cells, which comprise expression vectors that comprise the polynucleotide sequence of the nucleic acid molecule encoding the amino acid sequence of MGP-A, and a method for producing MGP-A by culturing such host cells. Consequently, it appears that all the limitations of the claims are met by the teachings of WO 97/29765-A1.

Although WO 97/29765-A1 does not explicitly teach that the nucleic acid molecule would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising the polynucleotide sequence set forth in SEQ ID NO: 1, because the polynucleotide sequence of the nucleic acid molecule is 100% identical to SEQ ID NO: 1 over the region spanning nucleotide residues 1 to 379, it would appear to one of ordinary skill in the art at the time the invention was made that the complement of the nucleic acid would hybridize under stringent or defined

hybridization conditions to a polynucleotide sequence comprising SEQ ID NO: 1. Therefore, the prior art nucleic acid molecule is deemed the same as the nucleic acid molecule of the instant claims, absent a showing of any differences. The office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics of the claimed product or would not function identically as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the Applicants to prove that the claimed nucleic acid molecule is functionally different than that taught by the prior art and to establish patentable differences.

20. Claims 1, 2, 6-9, 12-14, and 18-21 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kustikova, et al (*Genetika* 32: 621-628, 1996; Form PTO-1449, citation no. 11-AS) and Kustikova, et al (*Russian Journal of Genetics* 32: 540-546, 1996) or Kustikova (GenBank Accession No. X86374, 18 April 1995; Form PTO-1449, citation no. 11-AT).

Kustikova, et al and Kustikova teach the polynucleotide sequence of a nucleic acid molecule isolated from mouse that encodes a polypeptide comprising an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2, which is designated TAG7. Also, the nucleic acid molecule of Kustikova, et al and Kustikova encodes an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 20 to about 40 of SEQ ID NO: 2, an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 55 to about 75 of SEQ ID NO: 2, an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 90 to about 110 of SEQ ID NO: 2, and an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 145 to about 160 of SEQ ID NO: 2. Additionally, the nucleic acid molecule of Kustikova, et al and Kustikova is at least 65% identical to the polynucleotide sequence of SEQ ID NO: 1. Finally, Kustikova, et al teaches vectors that

comprise the polynucleotide sequence of the nucleic acid molecule encoding the amino acid sequence of TAG7. Consequently, it appears that all the limitations of the claims are met by the teachings of Kustikova, et al or Kustikova.

Although neither Kustikova, et al or Kustikova explicitly teach that the nucleic acid molecule would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising the polynucleotide sequence set forth in SEQ ID NO: 1, because the polynucleotide sequence of the nucleic acid molecule is 97.2% identical to SEQ ID NO: 1 over the region spanning nucleotide residues 1 to 549, it would appear to one of ordinary skill in the art at the time the invention was made that the complement of the nucleic acid would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising SEQ ID NO: 1. Therefore, the prior art nucleic acid molecule is deemed the same as the nucleic acid molecule of the instant claims, absent a showing of any differences. The office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics of the claimed product or would not function identically as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the Applicants to prove that the claimed nucleic acid molecule is functionally different than that taught by the prior art and to establish patentable differences.

21. Claims 1, 2, 6-9, 12, 13, and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Prokhortchouk (GenBank Accession No. Y12088, 01 April 1997).

Prokhortchouk teaches the polynucleotide sequence of a nucleic acid molecule isolated from mouse that encodes a polypeptide comprising an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2, which is designated TAG7. Also, the nucleic acid molecule of Prokhortchouk encodes an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 20 to about 40 of SEQ ID NO: 2 and an

epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 55 to about 75 of SEQ ID NO: 2. Additionally, the nucleic acid molecule of Prokhortchouk is at least 65% identical to the polynucleotide sequence of SEQ ID NO: 1. Consequently, it appears that all the limitations of the claims are met by the teachings of Prokhortchouk.

Although Prokhortchouk does not explicitly teach that the nucleic acid molecule would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising the polynucleotide sequence set forth in SEQ ID NO: 1, because the polynucleotide sequence of the nucleic acid molecule is 100% identical to SEQ ID NO: 1 over the region spanning nucleotide residues 1 to 248, it would appear to one of ordinary skill in the art at the time the invention was made that the complement of the nucleic acid would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising SEQ ID NO: 1. Therefore, the prior art nucleic acid molecule is deemed the same as the nucleic acid molecule of the instant claims, absent a showing of any differences. The office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics of the claimed product or would not function identically as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the Applicants to prove that the claimed nucleic acid molecule is functionally different than that taught by the prior art and to establish patentable differences.

22. Claims 1, 2, 6-9, 12, 13, and 19-21 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kang, et al (GenBank Accession No. AF076482, 08 July 1998).

Kang, et al teach the polynucleotide sequence of a nucleic acid molecule isolated from mouse that encodes a polypeptide comprising an amino acid sequence that is at least 65% identical to the amino acid sequence set forth in SEQ ID NO: 2, which is designated TAG7. Also, the nucleic acid molecule of Kang, et al encodes an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino

acid residues from about 20 to about 40 of SEQ ID NO: 2 and an epitope-bearing polypeptide comprising an amino acid sequence consisting essentially of amino acid residues from about 55 to about 75 of SEQ ID NO: 2. Additionally, the nucleic acid molecule of Kang, et al is at least 65% identical to the polynucleotide sequence of SEQ ID NO: 1. Consequently, it appears that all the limitations of the claims are met by the teachings of Kang, et al.

Although Kang, et al does not explicitly teach that the nucleic acid molecule would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising the polynucleotide sequence set forth in SEQ ID NO: 1, because the polynucleotide sequence of the nucleic acid molecule is 100% identical to SEQ ID NO: 1 over the region spanning nucleotide residues 1 to 248, it would appear to one of ordinary skill in the art at the time the invention was made that the complement of the nucleic acid would hybridize under stringent or defined hybridization conditions to a polynucleotide sequence comprising SEQ ID NO: 1. Therefore, the prior art nucleic acid molecule is deemed the same as the nucleic acid molecule of the instant claims, absent a showing of any differences. The office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics of the claimed product or would not function identically as the claimed nucleic acid. In the absence of evidence to the contrary, the burden is upon the Applicants to prove that the claimed nucleic acid molecule is functionally different than that taught by the prior art and to establish patentable differences.

Double Patenting

23. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re*

Ockert, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

24. A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

25. Claims 3 and 4 are rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 2 and 3, respectively, of prior U.S. Patent No. 6,172,211-B1. This is a double patenting rejection.

Claim 3 of this application is drawn to an isolated nucleic acid molecule comprising the polynucleotide sequence set forth in SEQ ID NO: 1. Claim 2 of '211 is also drawn to an isolated nucleic acid molecule comprising the polynucleotide sequence set forth in SEQ ID NO: 1. Although the claims are differently worded, the claims are limited to identical subject matter.

Claim 4 of this application is drawn to an isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence encoding amino acid sequence set forth in SEQ ID NO: 2. Claim 2 of '211 is also drawn to an isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence encoding amino acid sequence set forth in SEQ ID NO: 2. Although the claims are differently worded, the claims are limited to identical subject matter.

26. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

27. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

28. Claims 1-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,172,211-B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of claims 1-17 of this application encompasses the subject matter of claims 1-10 of '211 and because it would be obvious to one of ordinary skill in the art that the invention of claims 1-10 of '211 can be used to make the invention of claims 19-22.

Conclusion

29. No claims are allowed.

30. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Korobko, et al, Prokhorchuk, et al, Schibler, et al, Kusikova, et al, Marra, et al, De Tullio, NCI-CGAP, Bonaldo, et al teach polynucleotide sequences of isolated nucleic acid molecules and amino acid sequences of polypeptides that anticipate the subject matter of the present claims and could be used as bases for additional claim rejections under 35 USC §§ 102 and/or 103.

Art Unit: 1642

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.

Examiner

Art Unit 1642

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1330

slr

March 11, 2002

Notice to Comply	Application No.	Applicant(s)
	09/462,625	GEORGIEV ET AL.
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- 7. Other: Numerous discrepancies in the specificaiton and the Sequence Listing exist. Appropriate correction is required. If a substitute copy of the Sequence Listing and CRF is necessary to correct the errors, Applicants are required to also submit a statement the content of the paper and the CRF copies are the same and that neither include new matter.

Applicant Must Provide:

- An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

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